AAV9-Cas13 gene therapy for Angelman syndrome

Grant Award Details

AAV9-Cas13 gene therapy for Angelman syndrome

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-12577

Project Objective: To design and test, in rats and in patient-derived iPSC neurons, a Cas13 (RNA nuclease)-mediated gene therapy approach for Angelman syndrome (AS) in which the paternal UBE3A antisense RNA, which is expressed in neurons, is cleaved in such a way that paternal UBE3A expression is activated without activating other transcripts repressed by the antisense RNA.

Investigator:

Name:	David Segal
Institution:	University of California, Davis
Type:	PI

Disease Focus: Angelman Syndrome, Autism, Neurological Disorders

Human Stem Cell Use: iPS Cell

Award Value: $1,364,903

Status: Pre-Active

Grant Application Details

Application Title: AAV9-Cas13 gene therapy for Angelman syndrome

Public Abstract:

Research Objective

AAV9-Cas13 gene therapy for Angelman syndrome using a first-in-kind mechanism of action that will safely and permanently restore expression of endogenous UBE3A that is deficient in CNS neurons.

Impact

Angelman syndrome is a rare (1 in 15,000 births) neurogenetic disorder caused by loss of UBE3A in the brain, causing severe developmental delay, ataxia and epilepsy. There are no treatments or cures.

Major Proposed Activities

- Determine the optimal Cas13 guide-RNA for a rodent model.
- Determine the optimal Cas13 guide-RNA for a humans.
- Show that the gene therapy improves gene expression in rodent models.
- Show that the gene therapy improves gene expression in human cells.
- Show that the gene therapy improves symptoms in rodent models.
- Show that the gene therapy can be safe and permanent.

Statement of Benefit to California:

In addition to directly benefiting the ~2,500 children and families living with Angelman syndrome in California, this gene therapy with a first-in-kind mechanism of action could bring new treatments and new opportunities to our state. California has long been a hub of innovation, and creates an environment in which new technologies can be born, fostered, and attract others who want to create a better future for our residents. This activity will help train some of them, and inspire many others.

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